CLAIMS

I claim:

1. A method of alleviating a tumor in a human patient, the method comprising

i) locally administering to the tumor an antigen-releasing agent, whereby a tumor antigen is released from cells of the tumor;

iia) locally administering to the tumor a leukocyte attractant, whereby leukocytes are induced to infiltrate the tumor; and

iib) locally administering to the tumor interferon-gamma (IFN-g) and a second type 1 inflammatory response- (IR1-)promoting agent, whereby a type 1 inflammatory response is induced in the tumor and the tumor is alleviated.

2. The method of claim 1, wherein the antigen-releasing agent is a tumor de-bulking agent.

3. The method of claim 1, wherein the antigen-releasing agent comprises an agent selected from the group consisting of a proteolytic enzyme, an apoptosis-inducing agent, electrical current, a strong acid, and a strong base.

4. The method of claim 3, wherein the antigen-releasing agent comprises a proteolytic enzyme is selected from the group consisting of trypsin, chymotrypsin, pepsin, and collagenase.

5. The method of claim 3, wherein the antigen-releasing agent comprises only one proteolytic enzyme.

6. The method of claim 3, wherein the antigen-releasing agent comprises at least two proteolytic enzymes.

7. The method of claim 3, wherein the antigen-releasing agent comprises an alkylphospholipid.

8. The method of claim 7, wherein the alkylphospholipid is an alkylphosphocholine.

9. The method of claim 7, wherein the alkylphosphocholine is selected from the group consisting of hexadecylphosphocholine or edelfosine.

10. The method of claim 3, wherein the antigen-releasing agent is electrical current delivered by way of electrodes inserted into the tumor.

11. The method of claim 3, wherein the antigen-releasing agent comprises a strong acid selected from the group consisting of concentrated hydrochloric acid and concentrated sulfuric acid.

12. The method of claim 3, wherein the antigen-releasing agent comprises a strong base selected from the group consisting of concentrated sodium hydroxide and concentrated potassium hydroxide.

13. The method of claim 1, wherein the antigen-releasing agent is administered to the tumor at least two hours before administering the leukocyte attractant to the tumor.

14. The method of claim 1, wherein the antigen-releasing agent and the leukocyte attractant are co-administered to the tumor.

15. The method of claim 1, wherein the antigen-releasing agent is administered to the tumor at least two hours before administering IFN-g to the tumor.

16. The method of claim 1, wherein the antigen-releasing agent and the IFN-g are co-administered to the tumor.

17. The method of claim 1, wherein the leukocyte attractant comprises a monocyte attractant.

18. The method of claim 17, wherein the monocyte attractant is selected from the group consisting of MCP-1, MCP-2, MCP-3, and MCP-4.

19. The method of claim 1, wherein the leukocyte attractant comprises a T cell attractant.

20. The method of claim 19, wherein the T cell attractant is selected from the group consisting of RANTES, IP-10, and Mig.

21. The method of claim 1, wherein the leukocyte attractant comprises a granulocyte attractant.

22. The method of claim 21, wherein the granulocyte attractant is selected from the group consisting of interleukin-8, granular component P-2, growth-related oncogen-1, growth-related oncogen-2, growth-related oncogen-3, neutrophil activated protein, and neurotactin.

23. The method of claim 21, wherein the granulocyte attractant is a eosinophil attractant.

24. The method of claim 23, wherein the eosinophil attractant is eotaxin.

25. The method of claim 1, wherein the leukocyte attractant is co-administered with at least one of IFN-g and the second IR1-promoting agent.

26. The method of claim 1, wherein the leukocyte attractant and at least one of IFN-g and the second IR1-promoting agent are administered not more than two hours apart.

27. The method of claim 1, wherein the leukocyte attractant and at least one of IFN-g and the second IR1-promoting agent are administered more than two hours apart.

28. The method of claim 1, wherein the leukocyte attractant and at least one of IFN-g and the second IR1-promoting agent are co-administered.

29. The method of claim 1, wherein second IR1-promoting agent is selected from the group consisting of interleukin-2 (IL-2), interleukin-12 (IL-12), tumor necrosis factor-alpha (TNF-a), and tumor necrosis factor-beta (TNF-b).

30. The method of claim 29, wherein the second IR1-promoting agent comprises IL-2.

31. The method of claim 29, wherein the second IR1-promoting agent comprises TNF-b.

32. The method of claim 29, wherein the second IR1-promoting agent comprises both IL-2 and TNF-b.

33. The method of claim 1, wherein multiple aliquots of each of IFN-g and the second IR1-promoting agent are administered to the patient, and wherein at least 48 hours elapse between aliquots.

34. The method of claim 1, wherein IFN-g and the second IR1-promoting agent are co-administered.

35. The method of claim 1, wherein IFN-g and the second IR1-promoting agent are separately administered not more than two hours apart.

36. The method of claim 1, wherein IFN-g and the second IR1-promoting agent are separately administered more than two hours apart.

37. The method of claim 1, further comprising

iii) locally administering to the tumor a type 1 lymphocyte attractant in order to sustain the type 1 inflammatory response.

38. The method of claim 37, wherein the type 1 lymphocyte attractant is selected from the group consisting of RANTES, IP-10, and Mig.

39. The method of claim 37, wherein the type 1 lymphocyte attractant comprises IP-10 and Mig.

40. The method of claim 37, further comprising

iv) sustaining the type 1 inflammatory response by locally administering autologous leukocytes to the tumor.

41. The method of claim 37, further comprising

iv) administering a memory cell-inducing agent to the patient after inducing the type 1 inflammatory response, whereby production of anti-tumor type 1 immune memory cells is enhanced.

42. The method of claim 41, further comprising

v) supplementing the patient's nutrition with a nutrient selected from the group consisting of a vitamin and a mineral.

43. The method of claim 37, further comprising

iv) supplementing the patient's nutrition with a nutrient selected from the group consisting of a vitamin and a mineral.

44. The method of claim 1, further comprising

iii) locally administering autologous leukocytes to the tumor.

45. The method of claim 44, wherein the autologous leukocytes are obtained from the patient and expanded prior to locally administering them to the tumor.

46. The method of claim 44, wherein the autologous leukocytes are obtained from the patient and contacted with an IR1-promoting agent prior to locally administering them to the tumor.

47. The method of claim 44, wherein the autologous leukocytes are obtained from the patient, expanded ex vivo, and contacted with an IR1-promoting agent prior to locally administering them to the tumor.

48. The method of claim 47, wherein the leukocytes are contacted with both an IR1-promoting agent and with at least one of interferon-alpha (IFN-a) and IL-12 prior to locally administering them to the tumor.

49. The method of claim 44, further comprising

iv) administering a memory cell-inducing agent to the patient after inducing the type 1 inflammatory response, whereby production of anti-tumor type 1 immune memory cells is enhanced.

50. The method of claim 49, further comprising

v) supplementing the patient's nutrition with a nutrient selected from the group consisting of a vitamin and a mineral.

51. The method of claim 44, further comprising

iv) supplementing the patient's nutrition with a nutrient selected from the group consisting of a vitamin and a mineral.

52. The method of claim 1, further comprising

iii) administering a memory cell-inducing agent to the patient after inducing the type 1 inflammatory response, whereby production of anti-tumor type 1 immune memory cells is enhanced.

53. The method of claim 52, wherein the memory cell-inducing agent is selected from the group consisting of interleukin-15 (IL-15) and IFN-a.

54. The method of claim 52, wherein the memory cell-inducing agent is IL-15.

55. The method of claim 52, wherein the memory cell-inducing agent is IFN-a.

56. The method of claim 52, wherein the memory cell-inducing agent is administered after the tumor shrinks to less than 10 percent of its size immediately prior to administration of the antigen-releasing agent.

57. The method of claim 1, further comprising supplementing the patient's nutrition with a nutrient selected from the group consisting of a vitamin and a mineral.

58. The method of claim 57, wherein the vitamin is selected from the group consisting of vitamins A, B, C, D, and E.

59. The method of claim 58, wherein the vitamin is vitamin C and wherein the patient's nutrition is supplemented such that the patient receives from 200 to 400 milligrams of vitamin C daily.

60. The method of claim 58, wherein the vitamin is vitamin E and wherein the patient's nutrition is supplemented such that the patient receives from 200 to 400 international units of vitamin E daily.

61. The method of claim 57, wherein the mineral is selected from the group consisting of selenium, zinc, calcium, magnesium, iron, and copper.

62. The method of claim 61, wherein the mineral is selenium and wherein the patient's nutrition is supplemented such that the patient receives from 200 to 400 micrograms of selenium daily.

63. The method of claim 61, wherein the mineral is zinc and wherein the patient's nutrition is supplemented such that the patient receives from 15 to 100 milligrams of zinc daily.

64. The method of claim 57, wherein the patient's nutrition is supplemented beginning at least on the same day that the antigen-releasing agent is administered to the tumor, and continuing through at least the same day that IFN-g is administered to the tumor.

65. The method of claim 57, wherein the patient's nutrition is supplemented beginning at least five days before the antigen-releasing agent is administered to the tumor, and continuing through at least three days after the day that IFN-g is administered to the tumor.

66. A method of alleviating a tumor in a human patient, the method comprising

i) supplementing the patient's nutrition with a nutrient selected from the group consisting of a vitamin and a mineral;

ii) locally administering to the tumor an antigen-releasing agent, whereby a tumor antigen is released from cells of the tumor;

thereafter

iiia) locally administering to the tumor a leukocyte attractant, whereby leukocytes are induced to infiltrate the tumor; and

iiib) locally administering to the tumor interferon-gamma (IFN-g) and a second type 1 inflammatory response- (IR1-)promoting agent, whereby a type 1 inflammatory response is induced in the tumor;

thereafter

iv) sustaining the type 1 inflammatory response by

iva) locally administering to the tumor a type 1 lymphocyte attractant,

ivb) locally administering autologous leukocytes to the tumor, or

ivc) both iva) and ivb);

and thereafter

v) administering a memory cell-inducing agent to the patient after inducing the type 1 inflammatory response, whereby production of anti-tumor type 1 immune memory cells is enhanced and the tumor is alleviated.

67. A composition for alleviating a tumor in a human patient, the composition comprising IFN-g and a second IR1-promoting agent, whereby upon local administration of the composition to the tumor, a type 1 inflammatory response is induced in the tumor and the tumor is alleviated.

68. The composition of claim 67, wherein the second IR1-promoting agent is selected from the group consisting of IL-2, IL-12, TNF-a, and TNF-b.

69. The composition of claim 68, wherein the second IR1-promoting agent comprises IL-2.

70. The composition of claim 69, further comprising TNF-b.

71. The composition of claim 67, further comprising a leukocyte attractant.

72. The composition of claim 71, wherein the leukocyte attractant is selected from the group consisting of is selected from the group consisting of MCP-1,

MCP-2, MCP-3, MCP-4, RANTES, IP-10, Mig, interleukin-8, granular component P-2, growth-related oncogen-1, growth-related oncogen-2, growth-related oncogen-3, neutrophil activated protein, neurotactin, and eotaxin.

73. A kit for alleviating a tumor in a human patient, the kit comprising

i) an antigen-releasing agent;

ii) a leukocyte attractant; and

iii) IFN-g.

74. The kit of claim 73, further comprising

iv) an instructional material which describes administration of the antigen-releasing agent, the leukocyte attractant, and the IFN-g to the patient.

75. The kit of claim 73, wherein the IFN-g is in a composition which further comprises a second IR1-promoting agent.

76. The kit of claim 73, further comprising

iv) a type 1 lymphocyte attractant.

77. The kit of claim 73, further comprising one of

iva) a reagent for expanding lymphocytes ex vivo and

ivb) a reagent for differentiating lymphocytes ex vivo.

78. The kit of claim 73, further comprising

iv) a memory cell-inducing agent.

79. The kit of claim 73, further comprising

iv) a nutritional supplement.

80. The kit of claim 73, further comprising

iv) a type 1 lymphocyte attractant;

one of

va) a reagent for expanding lymphocytes ex vivo and

vb) a reagent for differentiating lymphocytes ex vivo;

vi) a memory cell-inducing agent; and

vii) an instructional material which describes administration of the antigen-releasing agent, the leukocyte attractant, and the IFN-g to the patient.